NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC™) GUIDELINE SYNTHESIS

SCREENING FOR AND MANAGEMENT OF CHLAMYDIAL INFECTION

Guidelines

1. Association for Genitourinary Medicine/Medical Society for the Study of Venereal Diseases (AGUM/MSSVD). 2002 national guideline for the management of *Chlamydia trachomatis* genital tract infection. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. [42 references].
2. Scottish Intercollegiate Guidelines Network (SIGN). Management of genital *Chlamydia trachomatis* infection. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2000 Mar. 26 p. (SIGN publication; no. 42). [176 references]
3. United States Preventive Services Task Force (USPSTF). Screening for chlamydial infection: recommendations and rationale. Am J Prev Med 2001 Apr;20(3S):90-4 [7 references]

INTRODUCTION:

A direct comparison of the Association for Genitourinary Medicine/Medical Society for the Study of Venereal Diseases (AGUM/MSSVD), Scottish Intercollegiate Guidelines Network (SIGN), and U.S. Preventive Services Task Force (USPSTF) recommendations for chlamydial infection is provided in the tables, below. The comparison focuses on screening for and management of chlamydial infection in adults. The evidence supporting the major recommendations is also identified, with the definitions of the rating schemes used by AGUM/MSSVD, SIGN, and USPSTF included in the last row of Table 2.

Following the content comparison table and discussion, the areas of agreement and differences among the guidelines are identified.

Abbreviations:

- AGUM/MSSVD, Association for Genitourinary Medicine/Medical Society for the Study of Venereal Diseases
- *C. trachomatis, Chlamydia trachomatis*
- DFA, Direct fluorescent antibody
- EIA , Enzyme immunoassay
- ELISA, Enzyme-linked immunosorbent assay
- GUM, Genitourinary Medicine
- HIV, Human immunodeficiency virus
- LCR, Ligase chain reaction
- NAAT, Nucleic acid amplification techniques

- PCR, Polymerase chain reaction
- PHE, Periodic health examination
- SIGN, Scottish Intercollegiate Guidelines Network
- STDs, Sexually transmitted diseases
- USPSTF, U.S. Preventive Services Task Force

TABLE 1: COMPARISON OF SCOPE AND CONTENT	
	OBJECTIVE AND SCOPE
AGUM/MSSVD (2002)	To present a national guideline for the management of *Chlamydia trachomatis* ge infection.

SIGN (2000)	• To present evidence-based recommendations for the prevention, diagnos treatment and management of chlamydial infection.
	• To specifically address the following questions:
	  • In which circumstances should potential chlamydial infection be s routinely in adults?
	  • What is the optimum management of patients identified as *Chlam trachomatis* positive?

USPSTF (2001)	• To make recommendations for screening for chlamydial infection. • To update the 1995 recommendations contained in the *Guide to Clinical Preventive Services*, second edition.
	TARGET POPULATION
AGUM/MSSVD (2002)	• United Kingdom • Men and women with *Chlamydia trachomatis* genital tract infection

SIGN (2000)	• Scotland
	• Individual patients presenting with signs and symptoms of genital chlamy infection.
	• Asymptomatic patients in the following specific circumstances:
	  • All women undergoing termination of pregnancy.
	  • All patients attending genitourinary medicine clinics.
	  • All patients with another sexually transmitted infection, including g warts.
	  • Sexual partners of those with chlamydial infection.
	  • Mothers of infants with chlamydial conjunctivitis or pneumonitis.
	  • Semen and egg donors.
	  • Sexual partners of those with suspected chlamydial infection.
	  • Women younger than 25 years and sexually active (targeted for opportunistic testing).
	  • Women aged 25 years or older with two or more partners in the la or a change of sexual partner in the last year (targeted for opport

	testing).
USPSTF (2001)	• United States • All sexually active women aged 25 years and younger • Asymptomatic pregnant women aged 25 years and younger • Other asymptomatic women at increased risk for infection • Asymptomatic men • High-risk young men
	INTENDED USERS
AGUM/MSSVD (2002)	Physicians
SIGN (2000)	Physicians; Nurses; Nurse Practitioners; Physician Assistants; Allied Health Care Practitioners; Students
USPSTF (2001)	Physicians; Nurses; Nurse Practitioners; Physician Assistants; Allied Health Care Practitioners; Health Care Providers
	INTERVENTIONS AND PRACTICES CONSIDERED
AGUM/MSSVD (2002)	*Diagnostic tests for chlamydial infection* 1. Cell culture 2. Direct fluorescent antibody (DFA) 3. Enzyme immunoassays (EIA) 4. Nucleic acid amplification techniques (NAAT) *Treatment/Management:* 1. Antibiotics • Doxycycline • Azithromycin • Erythromycin • Deteclo • Ofloxacin • Tetracycline 2. Patient education 3. Partner notification 4. Follow-up and test of cure
SIGN (2000)	*Diagnostic tests for chlamydial infection* 1. Cell culture. 2. Antigen detection. 3. DNA amplification tests (ligase chain reaction [LCR] or polymerase chain

	[PCR]). 4. Newer tests such as transcription-mediated amplification and strand-displ amplification are considered. *Treatment/Management* 1. Antibiotics • Azithromycin • Doxycycline • Lymecycline • Minocycline • Ofloxacin • Erythromycin • Amoxicillin • Doxycycline plus metronidazole (ofloxacin as an alternative to doxycycline; clindamycin as an alternative to metronidazole) • Oxytetracycline 2. Follow up and test of cure 3. Partner notification 4. Health education
USPSTF (2001)	Screening for chlamydial infection in the general population, certain high-risk grou in pregnant women using the following laboratory tests: 1. Cell culture 2. Antigen detection tests (direct fluorescent antibody assay and enzyme immunoassay) 3. Non-amplified nucleic acid hybridization, or newer technologies based on amplified DNA assays (polymerase chain reaction, ligase chain reaction, displacement assay, hybrid capture system, and transcription-mediated amplification of RNA)

TABLE 2: COMPARISON OF RECOMMENDATIONS FOR CHLAMYDIAL INFECTION	
Screening — Population Groups to be Screened	
	Routine screening of asymptomatic general population
AGUM/MSSVD (2002)	No recommendations offered
SIGN (2000)	No recommendations offered
USPSTF (2001)	No recommendation can be made for or against routinely screening asymptomati risk women in the general population for chlamydial infection. (**C recommendatic** The evidence is insufficient to recommend for or against routinely screening

	asymptomatic men for chlamydial infection. (**I recommendation**)
	Screening of asymptomatic high-risk groups
AGUM/MSSVD (2002)	No recommendations offered
SIGN (2000)	Testing for genital *Chlamydia trachomatis* infection should be performed in the fol specific circumstances: • All women undergoing termination of pregnancy. (**A recommendation**) • All patients attending genitourinary medicine clinics. (**B recommendatior** • All patients with another sexually transmitted infection (STI), including ge warts. (**B recommendation**) • Sexual partners of those with chlamydial infection. (**B recommendation**) • Mothers of infants with chlamydial conjunctivitis or pneumonitis. (**B recommendation**) • All women undergoing uterine instrumentation, including intrauterine devi insertion, who have risk factors for chlamydial infection. (**B recommenda** • Semen and egg donors. (**B recommendation**) • Sexual partners of those with suspected chlamydial infection. (**C recommendation**) Opportunistic testing could be considered in the following groups of women (**B recommendation**): • Women younger than 25 years and sexually active. • Women aged 25 years or older with two more partners in the last year or change of sexual partner in the last year.
USPSTF (2001)	It is strongly recommended that clinicians routinely screen all sexually active wom 25 years and younger, and other asymptomatic women at high risk for chlamydial infection. (**A recommendation**) *Clinical considerations*: • Women and adolescents through age 20 years are at highest risk for chla infection, but most reported data indicate that infection in prevalent amon aged 20-25. Age is the most important risk marker. Other characteristics associated with a higher prevalence of infection include being unmarried, American race, having a prior history of sexually transmitted disease, hav or multiple sexual partners, having cervical ectopy, and using barrier contraceptives inconsistently. • Clinicians should consider the characteristics of the communities they ser determining appropriate screening strategies for their patient population. • The optimal interval for screening is uncertain. For women with a previous negative screening test, the interval for re-screening should take into acc changes in sexual partner. If there is evidence that a woman is at low risk infection, it may not be necessary to screen frequently. Re-screening at 6 months may be appropriate for previously infected women because of hig

	of reinfection. • Screening of high-risk men is a clinical option. • Partners of infected individuals should be tested and treated if infected or presumptively.
	Screening of asymptomatic pregnant women
AGUM/MSSVD (2002)	No recommendations offered
SIGN (2000)	No recommendations offered
USPSTF (2001)	It is recommended that clinicians routinely screen all asymptomatic pregnant wom 25 years and younger and others at increased risk for infection of chlamydial infec **recommendation**) No recommendation can be made for or against routine screening of asympto low-risk pregnant women aged 26 years and older for chlamydial infection. (**C recommendation**) *Clinical considerations*: The optimal timing of screening in pregnancy is uncertain. Screening early in pregnancy provides greater opportunities to improve pregnancy outcomes, inc low birth weight and premature delivery; however screening in the 3rd trimeste more effective at preventing transmission of chlamydial infection to the infant c birth. The incremental benefit or repeated screening is unknown.
	Screening of patients with signs/symptoms of chlamydial infection
AGUM/MSSVD (2002)	No recommendations offered
SIGN (2000)	Testing for *Chlamydia trachomatis* should be performed in women and men with symptoms and signs which may be attributable to chlamydial infection (**B recommendation**): • Women — vaginal discharge, post coital/intermenstrual/breakthrough ble inflamed/friable cervix (which may bleed on contact), urethritis, pelvic inflammatory disease, lower abdominal pain in the sexually active, or reac arthritis in the sexually active • Men — urethral discharge, dysuria, urethritis, epididymo-orchitis in the se active, or reactive arthritis in the sexually active
USPSTF (2001)	Clinicians should remain alert for findings suggestive of chlamydial infection durin examination of asymptomatic women (e.g., discharge, cervical erythema, cervical friability).
Screening Tests	

	Types of screening tests
AGUM/MSSVD (2002)	• Ideal diagnostic test sensitivity is >90% with specificity >99%. The tests w most closely approach this are the nucleic acid amplification techniques (These perform better or at least as well as any of the other tests. • Only the better performing enzyme immunoassays (EIAs) should be usec sensitivities >80% and where sensitivity comparisons against NAAT techı have been carried out. • With EIAs, the technique of confirmation in the negative grey zone, either or NAAT, should be introduced. This improves sensitivity by 5-30%. • Quality control to validate the sensitivity and specificity of the assay used individual laboratories should be undertaken, in view of the reported wide the sensitivity of all tests. Both interlaboratory and intralaboratory control should be carried out, using both strong positives and negative and weak reactive specimens.
SIGN (2000)	The recommended laboratory test for *Chlamydia trachomatis* is a nucleic acid amplification test (e.g., ligase chain reaction [LCR] or polymerase chain reaction [(**B recommendation**)
USPSTF (2001)	A number of tests are available to identify chlamydial infection that use endocervi urethral swab specimens and urine specimens. Until recently, culture has been ac as the most specific test but it requires specialized handling and laboratory servic Antigen-detection tests (direct fluorescent antibody [DFA] assay and enzyme immunoassay [EIA]) and non-amplified nucleic acid hybridization, as well as newe technologies based on amplified DNA assays (polymerase chain reaction [PCR], chain reaction [LCR], strand displacement assay, hybrid capture system, and transcription-mediated amplification of RNA) may provide improved sensitivity, lov expense, availability, or timeliness of results over culture. New tests that use urine specimens provide a noninvasive method of screening both men and women. Sel administered vaginal and vulval-introital swabs using PCR and LCR, including sul samples by mail, are being used in research settings. The sensitivities and specifi nucleic acid amplification tests are all high, ranging from 82-100%. The sensitivity antigen detection tests (EIA, DFA) is slightly lower (70-80%) but specificity remair (96-100%).
	Specimen of choice
AGUM/MSSVD (2002)	*Women* Antigen detection techniques - EIA and DFA: • Cervical swab is the best specimen. • 10-20% additional positives will be detected by assaying a urethral specir well. This can be combined with the cervical specimen for analysis. Ureth swabbing suffers from the same disadvantages as in men. • Urine specimens perform significantly less well with EIA than cervical spe and are not recommended. • EIA should not be used for detecting *C. trachomatis* in the rectum or phar NAAT:

	• Cervical swabs consistently have sensitivities >80% • Urine has reported sensitivities of 44-94% • Vulvo-vaginal swabs have a sensitivity ≥85% Menstrual cycle and testing: • Preliminary data suggest that testing for *C. trachomatis* may detect more when undertaken in the latter part of the menstrual cycle. *Men* Antigen detection techniques - EIA and DFA: • First voided urine sample is as good as, if not better than, a urethral swab former is preferred because some patients find urethral swabbing painful tolerate it poorly and thus there is the potential for obtaining an inadequat specimen. Patients should hold their urine at least 1 hour before being tes preferably longer, as otherwise sensitivity is reduced (the optimum duratio known). • EIA should not be used for detecting *C trachomatis* in the rectum or phary NAAT: • First voided urine sample is the preferred specimen (see above).
SIGN (2000)	*Women* In women who are undergoing a vaginal examination, the specimen should be an endocervical swab. In women not undergoing a vaginal examination, a first void u should be obtained. A self-taken vaginal swab is an alternative specimen for wom cannot void urine at the time of visit. *Men* In men urethral swabs and first void urine have equal sensitivity, but urethral s causes discomfort. Therefore, in men, a first void urine is the sample of choice **recommendation**)
USPSTF (2001)	*Women* Endocervical swab specimens and first-void urine specimens had similar perform using DNA amplification tests. Urine tests allow noninvasive testing for women wi need for a pelvic examination thereby expanding opportunities for screening. *Men* Results of swab specimens compared to first-void urine specimens using DNA are similar. Although studies indicate that urine techniques are capable of impr sensitivity compared to culture, the importance of detecting and treating cultur negative infections is not yet known.
Management Recommendations	
	Antibiotic regimens in nonpregnant women and men

AGUM/MSSVD (2002)	Ideally, treatment should be effective (microbiological cure rate >95%), easy to ta more than twice daily), with a low side effect profile, and cause minimal interferen daily lifestyle (**C recommendation**). *Treatment of uncomplicated infection* Recommended regimens (**A recommendation**): • Doxycycline 100 mg twice a day for 7 days or • Azithromycin 1 g orally in a single dose Alternative regimens (**A recommendation**): • Erythromycin 500 mg four times a day for 7 days or • Erythromycin 500 mg twice a day for 14 days or • Deteclo 300 mg twice a day for 7 days or • Ofloxacin 200 mg twice a day or 400 mg once a day for 7 days or • Tetracycline 500 mg four times a day for 7 days Doxycycline and azithromycin (level of evidence Ia) These have been shown to have equal efficacy in clinical studies. Azithromyci considerably more expensive than doxycycline. Azithromycin may be particula in patients with erratic healthcare seeking behaviour. Ofloxacin (level of evidence Ib) It is unknown whether 200 mg twice a day is superior to 400 mg once a day. T no evidence to suggest that compliance with a once a day regimen is better th daily regimens. Whether missing a dose with 400 mg daily results in a less effi regimen than missing a dose with 200 mg twice daily is unknown. Ofloxacin ha efficacy to doxycycline and a better side effect profile but is considerably more expensive, so is not recommended as first-line treatment. Erythromycin (level of evidence Ib) Erythromycin is less efficacious than either azithromycin or doxycycline. When four times a day, 20-25% may experience side effects sufficient to cause the p discontinue treatment. There are only limited data on erythromycin 500 mg twi with efficacy reported at between 73-95%. A 2 week course appears to be mo efficacious than a 1 week course of 500 mg twice a day, with a cure rate ≥95%

	small study. Other tetracyclines (level of evidence Ib) Deteclo is probably as efficacious as doxycycline. However, photosensitivity o more frequently and there are not as many data on efficacy if compliance is p Tetracycline 500 mg is effective when taken four times a day for 7 days. Comp with such a regimen is likely to be poor, particularly in less motivated patients, whether such a regimen would then be efficacious is unknown. Oxytetracyclin four times a day has also been shown to be effective, although the published e is limited.
SIGN (2000)	Initiate treatment without waiting for laboratory confirmation of infection in patients symptoms and signs attributable to chlamydial infection and their sexual partners. **recommendation**) *Uncomplicated Infection* Uncomplicated genital *Chlamydia trachomatis* infection may be treated with ar the following, listed alphabetically (**A recommendation**): • Azithromycin 1g stat • Doxycycline 100mg twice daily for 7 days • Lymecycline 300mg once a day for 10 days • Minocycline 100mg once a day for 9 days • Ofloxacin 200mg twice daily for 7 days Taking into account the issue of compliance with therapy, it is recommended t uncomplicated genital *Chlamydia trachomatis* infection is treated with azithrom stat (**B recommendation**). *Upper genital tract infection in women (Chlamydial salpingitis/pelvic inflammat disease [PID])* The recommended treatment for upper genital tract infection in women is (**C recommendation**): • Doxycycline 100mg twice daily for a minimum of 10 days plus metronidaz 200mg three times a day or 400g twice daily for the first 7 days • Ofloxacin 400mg twice daily may be used as an alternative to doxycycline • Clindamycin 450mg four times a day may be used as an alternative to metronidazole *Upper genital tract infection in men (Chlamydial epididymo-orchitis)* The recommended treatment for upper genital tract chlamydial infection in me **recommendation**): • Doxycycline 100mg twice daily for 7-14 days or • Oxytetracycline 250mg four times a day for 7-14 days

USPSTF (2001)	No recommendations offered
	Antibiotic regimens during pregnancy and breast feeding
AGUM/MSSVD (2002)	• Doxycycline and ofloxacin are contraindicated in pregnancy. • The safety of azithromycin in pregnancy and lactating mothers has not ye fully assessed, although available data indicate that it is effective. • Erythromycin has a significant side effect profile and is less than 95% effe There are no trials of erythromycin 500 mg twice a day for 14 days, which be better tolerated than four times a day. • Amoxycillin had a similar cure rate to erythromycin in a meta-analysis and much better side effect profile. However, amoxycillin in vitro has been sho induce latency: there is therefore debate as to whether it is reliable. Regimens (Ia, **A recommendation**) • Erythromycin 500 mg four times a day for 7 days or • Erythromycin 500 mg twice a day for 14 days or • Amoxycillin 500 mg three times a day for 7 days Patients should have a test of cure 3 weeks after completing therapy.
SIGN (2000)	Uncomplicated genital chlamydial infection in pregnancy should be treated with (**A recommendation**): • Erythromycin 500mg four times a day for 7 days or • Amoxycillin 500mg three times a day for 7 days All women undergoing termination of pregnancy should receive antimicrobial t effective against chlamydial infection at the time of the procedure. (**A recommendation**)
USPSTF (2001)	No recommendations offered
	Patient education and preventive counseling
AGUM/MSSVD (2002)	In general, compliance with therapy is improved if there is a positive therapeutic relationship between the patient and the doctor. This can probably be improved if following are applied (**C recommendation**):

	Discuss with patient and provide clear written information on:
	
	• What chlamydia is and how it is transmitted:
	  • it is a sexually transmitted infection.
	  • if asymptomatic there is evidence that it could persist for months years.
	  • it can be isolated from the throat and eye without detectable infec the lower genital tract. It can therefore not always be assumed to sexually acquired.
	• The diagnosis of chlamydia, particularly:
	  • it is often asymptomatic especially in women
	  • while tests are accurate, no test is absolutely so.
	• The complications of untreated Chlamydia.
	• Side effects and importance of complying fully with treatment and what to dose is missed.
	• Interaction between antibiotics and oral contraceptive pill.
	• The importance of their sexual partner(s) being evaluated and treated.
	• Advice to abstain from sexual intercourse until they have completed thera their partner has been treated.
	• Advice on safer sexual practices.

SIGN (2000)	Sexual health promotion should be an integral part of contraception provision whe this is offered. • All patients with chlamydial infection should receive appropriate health ec including relevant reading materials (**B recommendation**). • Opportunities should be taken to deliver education in a wide variety of no care settings e.g., youth clubs, community centres, schools. Education ab chlamydia infection should be integrated with other sexual health educati condom promotion initiatives (**B recommendation**).
USPSTF (2001)	No recommendations offered
	Partner notification and treatment
AGUM/MSSVD (2002)	• All patients identified with *C. trachomatis* infection should be referred to d partner notification, where possible at initial diagnosis. • The method of partner notification agreed for each partner/contact identifi should be documented. • At subsequent follow up, partner notification outcomes should be ascertai documented. <u>Look back period</u> Only limited evaluation has taken place of the incubation period following expo the development of symptoms. In the United Kingdom an arbitrary cut off of 4 used to identify those sexual partner(s) potentially at risk if the index male pati symptomatic. As it is not known how long a patient can carry chlamydia

	asymptomatically, an arbitrary cut off of 6 months or until the last previous sex partner (whichever is the longer time period), is used in women and asymptom men. Common sense needs to be used in assessing which sexual partner(s) r been at risk in these situations. Those at risk should be informed and invited to for evaluation and epidemiological treatment even if tests are negative. This m patient led or provider led if the patient is unwilling to undertake it.
SIGN (2000)	Patients should be referred to trained health advisers for support with partner noti (**B recommendation**). Patients should be offered the choice of patient, provider or conditional referra partner notification (**B recommendation**): • Patient referral (or self referral): when index patients themselves inform th sexual contacts to seek treatment. • Provider referral: when the health care provider informs a patient's contac anonymously that they should seek treatment. This is obviously more tim consuming for the health care provider. • Conditional referral: where the health care provider notifies contacts if the has not done so after a given number of days. In men with symptomatic chlamydial infection, contact all partners over the fou prior to onset of symptoms (**C recommendation**). In women and asymptomatic men, contact all partners over the last six months most recent sexual partner (if out with that time period) (**C recommendation**).
USPSTF (2001)	Partners of infected individuals should be tested and treated if infected or treated presumptively.
	Follow-up
AGUM/MSSVD (2002)	This is an important part of the management of chlamydial infection. However, so patients may not return, emphasising the importance of the initial consultation. Fo has a number of objectives including: • Following up partner notification • Reinforcing health education • Providing reassurance • Assessment of treatment efficacy/exclusion of re-infection Patients do not need to be retested for *C. trachomatis* after completing treatme doxycycline or azithromycin unless symptoms persist or re-infection is suspect both are highly efficacious (**C recommendation**). A test of cure should be con 3 weeks after the end of treatment with erythromycin. A test of cure earlier will late failures and may detect non-viable organisms.
SIGN (2000)	Patients should be interviewed at follow-up with regard to compliance with therap risk of re-infection (**B recommendation**). In those patients who have been compliant with therapy in whom there is no ri

	reinfection, a test of cure need not be performed (**B recommendation**). Test of cure/re-infection established by molecular amplification assay should b performed a minimum of three weeks after the initiation of therapy, to avoid fal positive results (**B recommendation**).
USPSTF (2001)	No recommendations offered
Evidence Rating Schemes	
AGUM/MSSVD (2002)	**Levels of Evidence:** Ia — Evidence obtained from meta-analysis of randomised controlled trials Ib — Evidence obtained from at least one randomised controlled trial IIa — Evidence obtained from at least one well designed controlled study without randomisation IIb — Evidence obtained from at least one other type of well designed quasi-expe study III — Evidence obtained from well-designed non-experimental descriptive studies comparative studies, correlation studies, and case control studies IV — Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities **Grading or recommendations** A. (Evidence levels Ia, Ib): Requires at least one randomised controlled trial as part of the body of lit of overall good quality and consistency addressing the specific recommer B. (Evidence levels IIa, IIb, III): Requires availability of well conducted clinical studies but no randomised trials on the topic of recommendation. C. (Evidence level IV): Requires evidence from expert committee reports or opinions and/or clini experience of respected authorities. Indicates absence of directly applica studies of good quality.
SIGN (2000)	**Grades of Recommendations** A. Requires at least one randomised controlled trial as part of a body of liter overall good quality and consistency addressing the specific recommend (Evidence levels Ia, Ib) B. Requires the availability of well-conducted clinical studies but no randomi clinical trials on the topic of recommendation. (Evidence levels IIa, IIb, III) C. Requires evidence obtained from expert committee reports or opinions ar clinical experience of respected authorities. Indicates an absence of direc applicable clinical studies of good quality. (Evidence level IV) **Statements of Evidence** Ia — Evidence obtained from meta-analysis of randomised controlled trials. Ib — Evidence obtained from at least one randomised controlled trial. IIa — Evidence obtained from at least one well-designed controlled study with

	randomisation. IIb — Evidence obtained from at least one other type of well-designed quasi-experimental study. III — Evidence obtained from well-designed non-experimental descriptive stud as comparative studies, correlation studies, and case control studies. IV — Evidence obtained from expert committee reports or opinions and/or clin experiences of respected authorities.
USPSTF (2001)	USPSTF **grades its recommendations** according to one of five classifications (A D, or I), reflecting the strength of evidence and magnitude of net benefit (benefits harms). **A.** USPSTF strongly recommends that clinicians routine provide [the service] eligible patients. (The USPSTF found good evidence that [the service] improve important health outcomes and concludes that benefits substantially outweigh **B.** USPSTF recommends that clinicians routinely provide [the service] to eligil patients. (USPSTF found at least fair evidence that [the service] improves hea outcomes and concludes that benefits outweigh harms.) **C.** USPSTF makes no recommendation for or against routine provision of [the service]. (USPSTF found at least fair evidence that [the service] can improve h outcomes but concludes that the balance of benefits and harms is too close to general recommendation.) **D.** USPSTF recommends against routinely providing [the service] to asympto patients. (The USPSTF found at least fair evidence that [the service] is ineffec that harms outweigh benefits.) **I.** USPSTF concludes that the evidence is insufficient to recommend for or ag routinely providing [the service]. (Evidence that [the service] is effective is lack poor quality, or conflicting and the balance of benefits and harms cannot be determined.) USPSTF **grades the quality of the overall evidence** for a service on a 3-poi (good, fair, or poor). **Good** — Evidence includes consistent results from well-designed, well-conduc studies in representative populations that directly assess effects on health out **Fair** — Evidence is sufficient to determine effects on health outcomes, but the of the evidence is limited by the number, quality, or consistency of the individu studies; generalizability to routine practice; or indirect nature of evidence on he outcomes. **Poor** — Evidence is insufficient to assess the effects on health outcomes beca limited number of power of studies, important flaws in their design or conduct, the chain of evidence, or lack of information on important health outcomes.
TABLE 3: BENEFITS AND HARMS	
BENEFITS	
AGUM/MSSVD (2002)	These guidelines will aid in the appropriate diagnosis, treatment and managemen patients with *Chlamydia trachomatis* genital tract infection. This infection is comm

	5% of sexually active women attending United Kingdom general practice) and sus by unrecognised and thus untreated symptomless infection in both men and wom Complications cost at least 50 million pounds annually in the Untied Kingdom. Approximately 40% of non-gonococcal urethritis is caused by *C. trachomatis*.
SIGN (2000)	A guideline for the management of genital *Chlamydia trachomatis* infection has th potential to encourage the uptake of effective practice in the identification and trea chlamydial infection. Appropriate testing for chlamydial infections in defined clinica settings should lead to lower complication rates for individuals and in tandem with access to contact tracing, should lead to significant falls in re-infection rates and a reduced pool of infection within the community.
USPSTF (2001)	The strongest evidence supporting screening is a well-designed randomized trial demonstrating that screening women at risk (prevalence of infection 7%) reduced incidence of pelvic inflammatory disease from 28 per 1000 woman-years to 13 pe woman-years. The prevalence of chlamydial infection has declined in populations have been targeted by screening programs (primarily women attending family pla and other publicly funded clinics). In addition, two ecological analyses in Europe r reductions in ectopic pregnancy and pelvic inflammatory disease with the advent community-based screening for chlamydial infection. There is little evidence of the effectiveness of screening asymptomatic women who are not in high-risk groups. There is fair evidence indicating that screening for chlamydial infection among asymptomatic high-risk pregnant women and subsequent treatment improves pregnancy outcomes. Two non-randomized trial studies demonstrated improve pregnancy outcomes following treatment of chlamydial infection: less prematu rupture of membranes, less low birth weight, higher infant survival, and fewer s gestational age births. There is little evidence regarding the effectiveness of sc and treatment of asymptomatic pregnant women who are not in high-risk grou There is good evidence showing that treatment of men can eradicate chlamyd infection. Unfortunately, there are no studies describing the effectiveness of sc or early treatment of men in reducing acute infection and sequelae in men or v
HARMS	
AGUM/MSSVD (2002)	None stated
SIGN (2000)	None stated
USPSTF (2001)	No studies were identified that directly examined adverse effects of screening. Po harms include adverse effects of both false-positive and true-positive diagnoses o sexually transmitted disease on patients and their partners, the inconvenience of examinations for tests employing cervical specimens, and the potential harms of a reactions from antibiotic treatment. There may be added cost for confirmation of p results and testing of partners.

GUIDELINE CONTENT COMPARISON

The Association for Genitourinary Medicine/Medical Society for the Study of Venereal Diseases (AGUM/MSSVD), Scottish Intercollegiate Guidelines Network (SIGN), and U.S. Preventive Services Task Force (USPSTF) present recommendations for screening and management of chlamydial infection and provide explicit reasoning behind their judgments by ranking the level of evidence for each major recommendation.

USPSTF focuses on screening for chlamydial infection and is concerned mainly with the identification of the populations that are at highest risk for chlamydial infection and its complications. AGUM/MSSVD and SIGN address most aspects of chlamydial infection, including diagnosis, treatment, patient education, and follow-up. Unlike the other organizations, however, AGUM/MSSVD does not offer screening recommendations as this is the subject of ongoing research.

Areas of Agreement

Screening of Asymptomatic High-Risk Groups

SIGN and USPSTF offer recommendations on screening of certain asymptomatic high-risk populations for chlamydial infection. For instance, both groups agree that routine screening should be considered in sexually active women aged 25 years or younger. In addition, women of any age who change sexual partners are also considered at high risk for infection by both guideline groups. SIGN and USPSTF also agree that sexual partners of infected patients should be screened. Although AGUM/MSSVD does not make specific recommendations about screening, it does acknowledge risk factors for infection.

Screening of Patients with Signs/Symptoms of Chlamydial Infection

SIGN states that women with signs or symptoms of *C. trachomatis* infection (e.g., cervical discharge, cervical friability) should be tested for infection. USPSTF states that clinicians should be alert for signs and symptoms of infection during routine pelvic examination.

Types of Screening Tests

All three guideline groups agree that nucleic acid amplification tests (NAATs) are the most sensitive and specific diagnostic tests for chlamydial infection. NAATs include polymerase chain reaction and ligase chain reaction assays. NAATs have the additional advantage over other testing methods (cell culture, antigen detection) in that they can be performed on urine samples, thus eliminating the need for invasive testing. Although cell cultures have traditionally been held as the "gold standard," especially for medico-legal cases, NAATs have been shown to be more sensitive and easier to use than culture.

Specimen of Choice

The groups are in general agreement that endocervical swabs are the specimen of choice in adult women who are undergoing vaginal examinations for genital infection. First-void urine is recognized as an alternative for women unwilling or unable to undergo vaginal examination. All three guideline groups

agree that first-void urine is the specimen of choice for men when DNA amplification tests are used as screening tests.

Antibiotic Regimens in Nonpregnant Women and Men

AGUM/MSSVD and SIGN are in general agreement that uncomplicated genital chlamydial infection should be treated with tetracyclines (e.g., tetracycline, doxycycline, minocycline, lymecline, Deteclo); azithromycin; or ofloxacin. Single-dose azithromycin is acknowledged by all groups as the regimen of choice in patients who may be noncompliant with multi-dose regimens. Erythromycin is indicated only when other antibiotics are contraindicated or not tolerated by the patient.

Antibiotic Regimens during Pregnancy and Breast Feeding

AGUM/MSSVD and SIGN agree that either erythromycin or amoxicillin should be used to treat chlamydial infection in pregnant women or in women who are breast feeding.

Partner Notification and Treatment

AGUM/MSSVD, SIGN, and USPSTF acknowledge the need for referral of sexual partners for screening and possible treatment. AGUM/MSSVD and SIGN agree that in men with symptomatic chlamydial infection, all sexual partners over the four weeks prior to onset of symptoms are at risk for infection and should be referred. In women and asymptomatic men, all partners over the last 6 months should be referred.

Follow-up

AGUM/MSSVD and SIGN are the only two guidelines that offer recommendations on follow-up of patients after treatment. Both agree that retesting for *C. trachomatis* is not routinely necessary, unless noncompliance with therapy is suspected or patients are still symptomatic. AGUM/MSSVD does acknowledge, however, that retesting should be considered 3 weeks after the end of erythromycin treatment because it is less efficacious than doxycycline or azithromycin.

SIGN also emphasizes that any retesting should be done a minimum of 3 weeks after initiation of therapy to avoid false-positive results.

Patient Education and Preventive Counseling

AGUM/MSSVD and SIGN are in agreement that patients with chlamydial infections should be provided with information (including written material) on the nature of the chlamydial infection. Both guideline groups recommend counseling on safe sex practices, including condom use.

Areas of Differences

There are some differences among guidelines in the asymptomatic patient groups recommended for screening tests.

Screening of Asymptomatic High-Risk Groups

SIGN is the only guideline that recommends routine screening for the following patient groups: all women undergoing termination of pregnancy, all patients with another sexually transmitted disease (STD), all women undergoing intrauterine device (IUD) insertion, all patients attending genitourinary medicine (GUM) clinics, mothers of infants with chlamydial conjunctivitis or pneumonitis, and semen and eggs donors. To support its recommendation in women undergoing termination of pregnancy, SIGN cites evidence that shows that women seeking abortions are at increased risk of chlamydial infection and that failure to treat infection carries an approximately 25% risk of post-abortal salpingitis. SIGN acknowledges that no studies have specifically demonstrated the benefit of testing prior to IUD insertion, but 2 studies have shown that giving an antimicrobial agent effective against chlamydia at the time of IUD insertion reduced the rate of salpingitis. SIGN believes there is good evidence that attendees at GUM clinics and persons with other STDs have an increase likelihood of being infected with *Chlamydia trachomatis*, and that mothers of infants with chlamydial conjunctivitis or pneumonitis are likely to have genital chlamydial infection. Semen and egg donors should be tested for infection to reduce the risk of disease infection to the recipient.

Screening of Asymptomatic Pregnant Women

USPSTF is the only group that offers specific recommendations on routine screening of asymptomatic pregnant women. Specifically, USPSTF recommends screening only in pregnant women aged 25 years and younger and those at high risk of infection. The USPSTF found fair evidence that screening and treatment of women at high risk for chlamydial infections improves pregnancy outcomes, but it also found fair evidence that the benefits of screening low-risk pregnant women are small and may not justify the possible harms.

Routine Screening of Asymptomatic General Population

USPSTF evaluates evidence for routine screening of asymptomatic low-risk females, but they make no recommendations for or against routinely screening in this patient group. USPSTF found at least fair evidence that screening low-risk women can detect some additional cases of *Chlamydia trachomatis*, but they conclude that the potential benefits of screening low-risk women may be small and may not justify the possible harms.

USPSTF also evaluates routine screening of asymptomatic males for chlamydial infections, but conclude that the evidence is insufficient to recommend for or against routinely screening this patient group. USPSTF is the only group to specifically address these subpopulations.

This Synthesis was prepared by NGC on May 29, 2001. It was reviewed by the guideline developers on October 6, 2001. It was updated on February 20, 2002 following the withdrawal of the CTFPHC guideline from the NGC Web site. This Synthesis was most recently updated to incorporate 2002 updated recommendations from AGUM/MSSVD.

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